

Respiratory Institute



Cleveland Clinic

Staff Research Interests

Research Interest

Aboussouan, Loutfi

My research interests are in neuromuscular disease and in sleep medicine. From a neuromuscular perspective, I have been interested in the role of non-invasive ventilation in patients with ALS and its impact on survival, quality of life and rate of decline of lung function. More recently, I have been evaluating determinants of adherence to noninvasive ventilation that may be specific to the neuromuscular disorders (such as bulbar or cervical involvement). Other interests have included modeling the course of recovery of lung function in patients with diaphragm impairment.

Collaborative projects at the intersection of sleep and pulmonary medicine have been particularly rewarding. These include evaluations of exhaled nitric oxide or end-tidal CO₂ in patients with sleep apnea, with a particular focus on elements of the polysomnogram as potential determinants (such as apnea-hypopnea index, event and inter-event duration). New objective measures of CPAP adherence allow us to accurately assess determinants of compliance with my main interests centering on pulmonary parameters such as hyperinflation. The overlap syndrome (COPD and sleep apnea) is another area of research that combines sleep and pulmonary medicine. Tolerance of noninvasive ventilation or CPAP in such patients has been a topic of recent interest.

Aronica, Mark A.

Our lab focuses on the role of the Extracellular Matrix in asthma. The ECM was once thought to be inert scaffolding, having only a mechanical role in supporting and maintaining tissue structure. However, ECM has been shown to influence the distribution, activation status and survival, as well as adhesion of inflammatory cells and can act as a reservoir for inflammatory mediators and growth factors. The organization of the ECM induced by chronic inflammation may lead to alterations in airway structure and function, a process that has been referred to as remodeling in humans. This is of particular relevance in the asthmatic airways, in which the profile of ECM proteins is altered. Hyaluronan (HA) is an important component of the ECM normally found in adult tissues in small amounts but is present in higher amounts during wound healing. We utilize cell culture models, animal models of asthma, and correlate our findings with human samples to investigate the role of hyaluronan synthases and hyaluronan binding proteins as it relates to HA Synthesis and turnover in the lung and how this impacts inflammation, remodeling, and fibrosis.

Budev, Marie

The Cleveland Clinic lung and heart lung transplant program is active in a diverse group of innovative research programs including both multicenter and single center studies. There are many opportunities for fellow research in lung transplantation since it's a relatively new field with many unanswered questions. Below are areas of research interest for our team at this time some of which fellows can participate in and also we

encourage independent fellow projects as well. One of the key areas of interest for our transplant team is the area of antibody mediated rejection and we were the leading participant in multicenter NIH funded study HLA Antibodies After Lung Transplantation (HALT I) study evaluating long-term outcomes after early development of donor-specific HLA antibodies (DSAs) following lung transplant and the potential benefit of preemptive DSA depletion. Future funding for HALT II focused on treatment of DSA and AMR is currently awaiting funding. Internally, with both our thoracic pathology and immunology partners we are focusing on the long term outcomes of allograft that develop DSA and the variations in the pathology of AMR.

In the same arena, we are collaborating with Washington University in St. Louis on this NIH-sponsored trial to determine whether down regulation of autoimmune responses by depletion of autoantibodies to self-antigens prior to lung transplant will prevent primary graft dysfunction and reduce the risk of bronchiolitis obliterans syndrome and further work by our own labs looking at immune mechanism of rejection are continuing. A second area of interest in for our group is cytomegalovirus infection (CMV) and chronic lung allograft dysfunction (CLAD) and we will begin work in the Lung Transplant Clinical Trials Network (LT-CTN) CTOT – NIAID multicenter clinical trial in organ transplantation study which address two of the most important and current graft-limiting problems, cytomegalovirus infection (CMV) and chronic lung allograft dysfunction (CLAD) and aims to gain a better understanding the risks, phenotypes, and mechanisms of CLAD to reduce rates of long-term graft loss

Additional studies that lung transplant program staff are leading or taking part in include:

- A prospective study of the incidence, prevalence and risk factors for neurocognitive impairment in a cohort of lung transplant recipients.
- A multicenter trial assessing gastroesophageal reflux as a contributor to chronic lung allograft rejection
- A single center prospect investigation to determine the utility *pCLE (Probe based confocal laser endomicroscopy)* an optical tool, that allows *in vivo*, microscopic imaging of lung tissue during standard bronchoscopy looking for rejection after transplant

Chaisson, Neal

My interests focus largely on the intersection between pulmonary hypertension, hemodynamics, and education. Projects of potential interest to fellows include assessment of hemodynamic and PH education curricula in pulmonary and critical care training.

Culver, Daniel

My research mainly focuses on sarcoidosis and interstitial lung disease. Fellows might be involved in either clinical or experimental research. Prospective clinical research projects that may be feasible include use of corneal confocal microscopy in sarcoidosis, screening for small fiber neuropathy in chronic sarcoidosis, validation of an instrument

screening for small fiber neuropathy and the relationship of chronic sarcoidosis to cardiovascular disease using CT and biomarkers.

Duggal, Abhijit

My research interests are focused on the clinical epidemiology and outcomes associated with critical illness. I work mainly on outcomes research in ARDS and refractory Hypoxemia, and we are developing a database of patients with ARDS over the last 6 years. We are in the early phases of developing a registry of Severe Hypoxemic Respiratory Failure in patients being admitted to the Medical Intensive Care unit at Cleveland Clinic.

My current projects include

1. Prognostic factors associated with the development of refractory hypoxemia in Acute Respiratory Distress Syndrome (ARDS).
2. Variables associated with the use of non-conventional “rescue” ventilatory and non-ventilatory therapies in patients with refractory hypoxemia
3. Short and long term outcomes in patients with chronic respiratory diseases undergoing invasive mechanical ventilation
4. Epidemiologic characteristics of critical illness associated with viral pandemics
5. Outcomes associated with Therapeutic hypothermia in patients with Cardiopulmonary arrest

Dweik, Raed

Dr. Dweik’s research program draws on the strengths of the Department of Pulmonary and Critical Care Medicine in the Respiratory Institute (RI) and the Department of Pathobiology in the Lerner Research Institute (LRI). The overall goal of the Dweik lab is to understand lung physiology and pathology through the study of systemic and exhaled biomarkers. The strength of our research comes from its true translational nature and immediate clinical relevance. While our main area of interest is the pathobiology of pulmonary circulation (pulmonary hypertension), our work also covers lung physiology as well as the full spectrum of lung diseases that involve the airway (asthma), and the parenchyma (berylliosis-CBD).

Pulmonary Circulation: We have been conducting translational research in the area of nitric oxide (NO) biology and pulmonary vascular disease for the past 17 years and our current work is focused on the role of NO and the lung matrix (particularly Hyaluronan) in normal lung physiology and in the pathophysiology of pulmonary vascular and airway diseases.

Exhaled Breath Analysis: With each breath we exhale, thousands of molecules are expelled in our breath. Each individual has a “breath-print” that can tell a lot about his or her state of health. Our breath analysis laboratory continues to be at the cutting edge of this new field. Our most recent work focuses on the utility of exhaled breath analysis in

the identification and monitoring of lung (pulmonary hypertension, asthma, etc.) and systemic (heart, liver, GI, kidney, etc.) disease.

Erzurum, Serpil

The Erzurum lab studies airway Inflammatory diseases such as asthma, and pulmonary vascular diseases including pulmonary hypertension. Studies encompass basic science projects in the laboratory, translational projects with human samples, and clinical research trials.

Hatipoğlu, Umur

My research interests include respiratory mechanics, mechanical ventilation, outcomes research and COPD. I have had an open door policy for fellows who would like to get involved in my research projects. Recent graduates who have worked with me include Srinivas Mummadi, MD, Dileep Raman, MD, Manish Sharma, MD and Ahila Subramanian MD,PhD. The following are ongoing research projects.

- The influence of intrathoracic pressure on intravascular pressure in patients with suspected pulmonary hypertension
- IgE mediated asthma
 - Variability of total IgE over time in asthmatic patients
- Quality of care metrics
 - Risk prediction for readmissions to the hospital following an index admission of pneumonia
 - Factors that influence readmissions to the hospital for chronic obstructive pulmonary disease
 - Impact of a multidisciplinary COPD exacerbation clinic and care coordination program to quality of care
- Use of ultrasound in the ICU to facilitate utilization and cost savings
- COPD registry. An Oracle database is being built for the Cleveland Clinic to study clinical questions germane to COPD pathogenesis, risk factors, outcomes and population management in retrospective and prospective manner. The database will also be utilized to study quality metrics in the COPD care pathway.

Heresi Davila, Gustavo

My research focuses on pulmonary arterial hypertension, particularly in the areas of biomarkers and prediction of clinical outcomes.

There are several potential projects based on our large PH database, for example we are looking into novel clinical predictors of outcome and at the clinical features of patients with borderline pulmonary pressures.

We collect blood samples and we are measuring several novel biomarkers of the disease, like CRP, chemokines and HDL-cholesterol.

We are interested in the role of insulin resistance in pulmonary vascular disease. We have a funded project to begin shortly where we will perform a detailed metabolic profiling of patients with idiopathic PAH.

Highland, Kristin

My research focuses on rheumatic lung disease with an emphasis on interstitial lung disease and pulmonary hypertension.

Hite, R. Duncan

The overall goal of my research activities is translational research in critical care medicine, and includes the following general areas:

- Cellular/Molecular: studies investigating mechanisms of surfactant injury triggered by acute lung inflammation. In particular, we focus on upregulation of secretory phospholipases and phospholipase-mediated surfactant depletion and dysfunction. Specific diseases of interest include acute lung injury, asthma and more.
- Clinical Trials: Studies are focused on observational interventional studies focused on acute lung injury, sepsis, pneumonia, delirium and more. Current active studies include federal and industry funded multicenter trials on ARDS (including the PETAL Network), sepsis and pneumonia. The Cleveland Clinic serves as one of 12 primary sites for the NIH-funded PETAL Network which focuses on trials on prevention and early treatment of ARDS. As a primary site, the Cleveland Clinic serves to coordinate the activities of 4 hospitals across Ohio including Ohio State University, University of Cincinnati and Akron City Hospital along with our hospitals in the Cleveland area. Involvement in these activities provides excellent opportunities and resources for small ancillary studies that take advantage of databases and clinical samples from each trial.
- Quality Improvement: Projects designed to determine optimal approaches to the delivery of care to patients in the ICU using rapid cycle approaches that combine with available Institute statistical and IT resources. Projects in the past have included prevention of VAP, ICU sedation, delirium management, ventilator management, weaning, palliative care and more.

Khatri, Sumita

Research interests include air pollution and health (asthma), health disparities in outcomes and delivery of care for asthma, bronchial thermoplasty for asthma, biomarkers of asthma and airway inflammation, vocal cord dysfunction and asthma.

The USEPA has recently completed an in-depth air quality study on the characteristics and sources of particulate matter (soot) pollution in the area. We are currently

collaborating with them on an epidemiologic health study evaluating particulate matter (PM) pollution and presentations for acute asthma (data on acute MI is also available). Geographic information systems (GIS) is used to estimate individual exposures to air pollution prior to their presentations for asthma to determine whether there are patterns of exposure related to such presentations. Ancillary studies from this collaboration are possible.

The Asthma Care Paths have created an opportunity for collaboration in the care of asthma not seen before here at Cleveland clinic. This allows us to get a sense of prior practice patterns, and evaluate how having a more protocolized approach may help patients with asthma and change outcome metrics across the institution. Further, high risk individuals and groups with asthma exist in our community, and best practices for the breaking down of barriers for the care of asthma need to be implemented and evaluated for efficacy.

The Bronchial Thermoplasty and Registry Study proposes the formation of a 3-year registry with evaluation of clinical, physiologic, biologic, and imaging results that may predict clinical response to bronchial thermoplasty in patients with severe refractory asthma.

Dr Claudio Milstein (Voice Center) has a large patient experience with vocal cord dysfunction and breathlessness. We are planning on writing up the Cleveland Clinic Speech Center/Asthma Center experience with these patients, looking for research questions as well.

Mazzone, Peter

Research focus in the lung cancer program would relate to an area of lung cancer that we as pulmonologists play a major role in. These are many, and there are many unanswered questions in these areas, leading to the possibility of a wealth of research. There are opportunities for both clinical and translational research projects.

1. Epidemiology
 - prediction of the risk of developing lung cancer (clinical, genetic, molecular)
 - gender differences
 - health care disparities
 - presentation
2. Primary Prevention
 - smoking cessation
 - chemoprevention
3. Secondary Prevention (lung cancer screening)
 - imaging programs
 - biomarker development and validation (risk, diagnosis, evaluation of nodules)
4. Diagnosis and Staging
 - lung nodule management (imaging advances, biomarker development and validation)

- bronchoscopic advances
- 5. Pre-operative Evaluation of the Lung Resection Candidate
 - algorithms, other forms of exercise testing
 - development of risk predictor indices
 - guidelines assessment
 - interventions (pulmonary rehab, smoking cessation, etc.)
- 6. Follow-up Post Curative Intent Treatment and Tertiary Prevention
 - no defined protocols for follow-up – imaging, biomarker development and validation
 - outcomes research – surgery, chemo/XRT
 - quality of life
 - chemoprevention

Mehra, Reena

My research focus involves exploring pathways mediating the relationship between sleep disordered breathing and cardiac electrophysiology as well as cardiovascular disease from a clinical trials and epidemiologic perspective. For over 10 years I have led and administered several NIH funded and foundation grant projects including a de novo analyses of electrophysiologic signals in large-scale epidemiologic cohorts, the Sleep Heart Health Study and Outcomes of Sleep Disorders in Older Men study, involving thousands of participants with the goal of investigating relationships of sleep apnea and nocturnal cardiac arrhythmias. I have also led the conduct of a parallel randomized controlled trial evaluating the effects of sleep apnea treatment on biomarkers of oxidative stress. My recent research is focused on honing in on underlying pathophysiologic mechanisms linking sleep apnea and paroxysmal atrial fibrillation and investigating the longitudinal relationships of polysomnographic and electrophysiologic markers with the development of incident atrial fibrillation. Students, residents and fellows have worked with our research team on various projects including clinical trials design in sleep apnea, predictors of positive airway pressure adherence, prevalence of newly diagnosed insulin resistance in a sleep apnea clinical trial, relationship of central versus obstructive apnea and incident atrial fibrillation and the impact of sleep apnea treatment on biomarkers of systemic inflammation and vascular function.

Mehta, Atul C.

Research interests and projects are:

1. Endobronchial Volume Reduction: Coil Trial, Crossover-Coil Trial
2. Bronchoscopic Decompression for Emphysema
3. Role of Lung Transplantation in Excessive Dynamic Collpase
4. Tracheobronchopathia Osteochondroplastica

Mireles-Cabodevila, Eduardo

Research interests and projects are:

1. Mechanical ventilation: application, nomenclature, patient-ventilator interaction, prolonged mechanical ventilation.
 - a. I work with simulators to assess ventilator and mode performance.
 - b. Improving the delivery of mechanical ventilation by establishing algorithms
2. Neuromuscular disease: Respiratory muscle involvement, optimizing care, respiratory and ventilator support, diaphragmatic pacing.
 - a. I am working on how to improve respiratory care of these patients, in and outside the hospital.
 - b. What is the rate of progression of the disease and timing for optimal interventions
3. Critical Illness: I am interested in critical care in general, I have special interests in education, liver failure and sepsis.
 - a. I am doing research on the effect of simulation in education and patient outcomes

Scheraga, Rachel

My research interests as part of Dr. Mitchell Olman's lab are focused on the lung biology of idiopathic pulmonary fibrosis (IPF) and acute lung injury. Specifically, I am studying the role of the transient receptor potential vanilloid (TRPV4) channel in the macrophage. We hope to determine the function of this channel in the macrophage as it could be a potential drug target to treat IPF and other lung diseases.

Southern, Brian

My research focus is fibroblast/myofibroblast signaling in idiopathic pulmonary fibrosis (IPF). Specifically, I am interested in what signals drive fibroblast/myofibroblast activation and accumulation in areas of ongoing fibrosis in the lung.

Our lab has developed a novel system that allows us to study the fibroblast-matrix interactions in normal and fibrotic lung tissue. With this model, we have shown that fibroblasts preferentially adhere to fibrotic lesions, become immotile, and differentiate into myofibroblasts. Myosin II appears to be a critical molecule which can perform different functions depending on whether the fibroblast is interacting with normal or fibrotic lung. I am currently working on better defining this mechanism and exploring ways to manipulate myosin II activity to interrupt the fibroproliferative cycle.

Opportunities are always available in Dr. Mitch Olman's laboratory for fellows interested in basic science or translational research in IPF.

Stoller, James

Research interests regard alpha-1 antitrypsin deficiency, health care delivery of respiratory care services, the impact and outcomes of education, leadership development activities, and optimal educational strategies (e.g., in simulation, etc.). The experience of collaborating with me will offer experience perspectives on clinical

research design as well as the mechanics of writing, submitting, and editing research papers.

I am also absolutely available to fellows to help them prepare reviews of clinical issues and on academic mentorship issues.

Tonelli, Adriano

Research interests include the study of systemic vascular function and hemodynamics including invasive and non-invasive cardiac output determinations in pulmonary vascular diseases. I am particularly interested in the study of pulmonary hypertension in patients with liver diseases. In addition, I am attracted to perform electro or echocardiographic studies in patients with a variety of lung diseases.

Tsuang, Wayne

Research interests include leveraging large databases for lung transplant outcomes research. I have been working with Maryam Valapour MD, MPP to review the allocation efficiency of donor lungs in the U.S. with data from the Scientific Registry of Transplant Recipients (SRTR). Other projects include the Clinical Trials in Organ Transplant grant (CTOT), funded by the National Institute of Allergy and Infectious Diseases, a multicenter clinical trial group that will focus on creating a registry of patients with Chronic Lung Allograft Dysfunction (CLAD) and also enroll patients in clinical trials evaluating the prevention and treatment of cytomegalovirus (CMV) post-transplant. Finally, using single center data I am studying at the importance of intravenous immunoglobulin supplementation for hypogammaglobulinemia in lung transplant patients.

Valapour, Maryam

My research is focused on the study of lung transplant outcomes. On the national level, I serve as the Senior Investigator for Lung Transplant for the Scientific Registry of Transplant Recipient (SRTR). At the SRTR, I oversee the analysis of US lung transplant data and refinement of the US lung allocation system. I am also working to develop projects to study outcomes of lung transplant at the Cleveland Clinic, one of the largest lung transplant programs in the US.

Zein, Joe

My research interest is focused on large databases, health economics, asthma epidemiology and the role of aging and gender on asthma severity. I am also interested in precision medicine and genetic epidemiology.

Publications

Aboussouan, Loutfi

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